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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,035	10/07/2003	Mariann Pavone-Gyongyosi	ARTHP118US	5279

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EXAMINER	
BRADLEY, CHRISTINA	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
12/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/680,035	PAVONE-GYONGYOSI ET AL.	
	Examiner	Art Unit	
	CHRISTINA BRADLEY	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 29* is/are pending in the application.

4a) Of the above claim(s) *1-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26, 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-26 and 29 are pending. Claims 27, 28 and 30 were cancelled in the response filed 12/02/2010. Claims 1-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. In the response filed 12/02/2010, Applicant cancelled all previously claimed species and added a new set of species to claim 22. Because prior art on the species listed in the rejection under 35 USC 102(b) below was , the search was not extended in accordance with MPEP § 803.02.

Claim Objections

2. Claims 22-26 and 29 are objected to for improper Markush language. The claim should read "selected from a group consisting of" not "selected from a group comprising". See MPEP § 2173.05(h).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24-26 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the definition for variables R and X in the formula R-Lys-X. The amendment filed 12/02/2010 overcomes this rejection only for claims 22 and 23 because only these claims were amended to include definitions for the variables R and X.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of claims 22-30 under the written description provision of 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment filed 12/02/2010.

7. Claims 22-26 and 29 are rejected under 35 U.S.C. 112, first paragraph because the specification does not reasonably provide enablement for the use of stents coated with compounds of formula R-Lys-X. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. It is noted that the species KKKKK, which is the subject of the prior art rejections over Hill-West et al. below, is excluded from this rejection.

8. To comply with the enablement requirements of 35 U.S.C. §112, first paragraph, a specification must adequately teach how to make and how to use a claimed invention throughout its scope, without undue experimentation. *Plant Genetic Systems N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339, 65 USPQ2d 1452, 1455 (Fed. Cir. 2003). There are a variety of factors which may be considered in determining whether a disclosure would require undue experimentation. These factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art,

(7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Nature of the Invention

9. The claims are drawn to hemocompatible stents coated with compounds of formula R-Lys-X and methods of manufacture. According to the specification, the purpose of the coating is to reduce the risk of restenosis.

Breadth of the Claims

10. The claimed stents are coated with compounds of formula

R-Lys-X

wherein

R is hydrogen, an acyl or acetyl group, an amino acid or a peptide with 2-70 amino acids; and X is a hydroxyl, amino, monoalkyl, dialkyl or alkoxy group, an amino acid or an oligopeptide selected from the group comprising Pro, Pro [TVARNDCEQGHILKMFPSW], Pro-Thr-[TVARNDCEQGHILKMFPSW] and Pro-Val-[TVARNDCEQGHILKMFPSW].

Thus, the formula includes the single amino acid lysine, peptides from 2 to 71 amino acids long with lysine as the C-terminal residue, peptides from 2 to 72 amino acids long with Lys-Pro as the C-terminal residues, and peptides from 2 to 73 amino acids long with Lys-Pro-Xaa or Lys-Val-Xaa as the C-terminal residues, which together constitute a countless number of species. The core structure common to the entire genus is lysine either as a single amino acid or as a C-terminal residue. Thus, any function of the genus must be attributed to this core.

11. In the arguments filed 12/02/2010, Applicant states that the claimed formula is limited to compounds "having a high similarity to SYSMEHFRWCKPV" (α-melanocyte stimulating

hormone or αMSH). Clearly, species of the formula such as the single amino acid lysine and a 71 amino acid peptide terminating in lysine but sharing no other homology to αMSH, do not have a high level of structural or functional similarity to αMSH. Therefore, it is not accurate to characterize the claimed genus as peptides with close similarity to αMSH.

Unpredictability of the Art

12. With respect to the intended use of restenosis inhibition, there is a high level of unpredictability in the art. Slavin et al. ("Drug-eluting Stents: Preventing Restenosis," *Cardiology in Review*, **2007**, *15*, 1-12) outline the state of the field: "Overshadowing the early success of angioplasty was the high rate of angiographic restenosis and recurrent symptoms at 6 months. The use of stents reduced the incidence of restenosis; however, the rise in the number of patients undergoing percutaneous interventions produced a new problem of restenosis occurring within the stent: in-stent restenosis (ISR). Mechanical approaches, including directional and rotational atherectomy and systemic pharmacotherapy, have failed to demonstrate a reduction in ISR in randomized clinical trials. Intravascular brachytherapy is currently the only approved therapy for ISR, although this treatment has numerous unresolved questions and is not effective in a large percent of patients. Drug eluting stents have reduced the incidence of restenosis by providing localized therapy to the targeted lesion without systemic toxicity." Slavin et al. teach although many agents were tested in the preclinical analysis, only two have demonstrated success at reducing restenosis, sirolimus and paclitaxel (p. 3, col 2).

13. There is no report in the prior of αMSH or related peptides to reduce restenosis.

Working Examples

14. The specification fails to disclose a single working example of a stent coated with a compound of formula R-Lys-X.

15. The specification fails to provide experimental data pertaining to the use of αMSH or related peptides to reduce restenosis.

Guidance in the Specification

16. The instant specification fails to provide guidance on how to choose a compound of the formula R-Lys-X that is capable of reducing restenosis. The specification does not disclose, for example, which structural elements are critical for this function. Applicant's argument that the genus is limited to compounds with close similarity to αMSH is unpersuasive because neither the specification or the prior art demonstrate that αMSH can be used for this purpose. Furthermore, the specification does not provide sufficient guidance to permit one of ordinary skill in the art to determine the definition of "close similarity".

17. Furthermore, the breadth of the genus R-Lys-X is so extensive that it must include compounds with a diverse array of functions, none of which are disclosed, and which may or may not include an ability to reduce restenosis. The specification fails to provide guidance on how to use compounds of R-Lys-X that have no impact on restenosis but which likely constitute a large portion of the genus.

Experimentation Required to Practice the Invention

18. Considering the factors above, the skilled artisan would be burdened with undue experimentation in determining if one of the claimed medical products would be effective at inhibiting restenosis, or finding an alternative use for the product. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention

without undue experimentation. Therefore, in view of the *Wands* factors, the claims appear to require undue experimentation to use the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. The rejection of claims 29 and 30 under 35 U.S.C. 102(e) as being anticipated by Bell (US 2004/0219147) is withdrawn in view of the amendment filed 12/02/2010.

21. The rejection of claims 22-25, 28 and 29 under 35 U.S.C. 102(b) as being anticipated by Chluba et al. ("Peptide Hormone Covalently Bound to Polyelectrolytes and Embedded into Multilayer Architectures Conserving Full Biological Activity," *Biomacromolecules*, **2001**, *2*, 800-805) is withdrawn in view of the amendment filed 12/02/2010.

22. Claims 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Hill-West et al. (WO 02/17880). Hill-West et al. teach stents coated with macromers comprising biocompatible, biodegradable polymers and the peptide KKKKK, which function to release and produce NO (p. 9, lines 14-20, p. 11, line 28 - p. 15, line 3, p. 23, lines 9-11, Example 2, Example 7, Figure 4, claims 13 and 25).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. The rejection of claims 22, 26 and 27 under 35 U.S.C. 103(a) as being unpatentable over by Bell (US 2004/0219147) is withdrawn in view of the amendment filed 12/02/2010.

25. Claims 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill-West et al. (WO 02/17880). Hill-West et al. teach stents coated with macromers comprising biocompatible, biodegradable polymers and the peptide KKKKK, which function to release and produce NO (p. 9, lines 14-20, p. 11, line 28 - p. 15, line 3, p. 23, lines 9-11, Example 2, Example 7, Figure 4, claims 13 and 25). It would have been obvious to make the stent coated with the macromer comprising the peptide KKKKK taught by Hill-West et al. by a) providing the stent, and b) coating it with the macromer comprising KKKKK, satisfying claim 22. With respect to claims 23-26, Hill-West et al. teach that multiple macromers can be used including those comprising PEG, a biodegradable polymer, and an active agent such as NO or a cell adhesion ligand (claims 12-14 and 19). A method of applying multiple macromers would

comprise steps of applying a biodegradable polymer (i.e. PEG) prior to or after the application of the KKKKK-containing macromer. With respect to claim 26, it would have been obvious to combine the KKKKK-containing macromer with other agents such as NO or a cell adhesion ligand. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

26. No claims are allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BRADLEY whose telephone number is (571)272-9044. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 8:30 A.M. to 4:30 P.M.

29. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christina Marchetti Bradley/
Primary Examiner, Art Unit 1654

cmb